

**REMARKS****CLAIM REJECTIONS UNDER 35 U.S.C. § 101**

Claims 1-14 were rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The Examiner states "the computation steps/processes of claims 1-14 are merely 'mental' processes of performing mathematical operations (manipulation of numbers) applied to a computer. The claims do not recite any concrete or tangible results; therefore the claims do not recite statutory subject matter."

Applicants respectfully direct the Examiner to the most recent U. S. Supreme Court authority on patent eligible subject matter, *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred International, Inc.*, 534 U.S. 124, 122 S.Ct. 593 (2001) noting that the language of § 101 is extremely broad. In addition, that same Court also recognized that § 101 is a dynamic provision designed to encompass new and unforeseen inventions. Therefore, the U.S. Supreme Court's most recent articulation of 35 U.S.C. § 101 appears to provide for a broader view of patentable subject matter than that which the Examiner articulates. However, in order to expedite allowance of the application, claim 1 has been amended to recite in part "[a] computer-based directed evolution method". Support can be found in the application as filed. Applicants respectfully submit that the source code, stored by the computer, as shown starting on page 26 provides a concrete tangible result.

Although not acceding to the Examiner's rejection, claim 2 has been cancelled. Claim 3 has been amended to depend from independent claim 1. Claims 3-10 by virtue of their dependency contain all the limitations of the claim from which they depend.

Claim 11 has been amended to recite "an *in vitro* method of providing an isolated nucleic acid molecule derived from a directed evolution experiment", thereby reciting a tangible result.

## CLAIM REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-15 were rejected under 35 U.S.C. § 112, first paragraph as the Examiner states "the specification does not reasonably provide enablement for the method and modeling the directed evolution protocol by any other means. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with these claims."

Applicants respectfully traverse this rejection. As long as the specification discloses at least one method for making and using the claimed invention if there is a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. *In re Fischer*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. § 112. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533, 3 U.S.P.Q.2d 1737-1743 (Fed. Cir.), *cert. denied*, 484 U.S.C. 54 (1987). Applicants submit the enablement requirement is satisfied because the specification discloses at least one method of modeling a directed evolution protocol that is commensurate with the claims; therefore, the specification is not required to show it by any other means as alleged by the Examiner. Applicants respectfully request this rejection be withdrawn.

The Examiner states "claim 10 is not commensurate in scope with the specification with regard to the instantly claimed step where the 'assembly algorithm excludes silent crossovers'". Furthermore, the Examiner states "no other methods are taught for excluding silent crossovers are disclosed in the specification provides no guidance as to other methods for excluding silent crossovers."

Applicants respectfully traverse this rejection. As stated above, as long as the specification discloses one method for making and using the claimed invention there is a reasonable correlation to the entire scope of the claim, then the enablement requirement under § 112 is satisfied. Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. § 112. The specification discloses that "the annealing of a fragment  $m$  to a growing template ending with a fragment from parent  $k$  is equivalent to the continuation of the template with nucleotides from parent  $k$ , no crossover is counted". (See page 13, lines 13-22 and page 17, lines 13-16). Applicants submit the enablement requirement is satisfied because the specification discloses at least one method of excluding silent crossovers that is commensurate in scope with the specification; therefore, the specification is not required to show any other means as alleged by the Examiner.

#### CLAIMS REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-15 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states "claims 1,15, and all claims dependent therefrom are indefinite due to the lack of clarity of the claim language failing to recite a final process step which agrees back with the preamble." "There is no indication of a modeling step or recited in the preamble. Clarification of the metes and bounds of the claim is requires, via clearer claim wording."

Applicants have amended claim 1 in order to recite a final process step that agrees back with the preamble. With respect to claim 15, Applicants have amended the claim to recite "in order to model the directed evolution protocol" in order to recite a final process step which agrees back with the preamble.

The Examiners states "claims 12 and 13 recite 'wherein a vector' or 'wherein a host cell', respectively, which is confusing. It is unclear as to the limitations dependent claims 12 and 13 provide for because said claims are directed to a physical limitation (i.e. vector and host cell). In contrast, claim 11 is interpreted to be directed to a computational/*in silico* method where the nucleotide sequence is a character string rather than an actual piece of DNA. Clarification of the metes and bounds, via clearer claim language, is requested."

Applicants have amended claim 11 to recite "an *in vitro* method of providing an isolated nucleic acid molecule derived from a directed evolution experiment", to clearly indicate that claim 11 is to be interpreted to be directed to an *in vitro* method where the nucleotide sequence is an actual piece of DNA. Claims 12-14, by virtue of their dependency contain all the limitations of the amended independent claim 11.

#### CLAIM REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-15 were rejected under 35 U.S.C. § 102(a) as being anticipated by Moore et al.

Applicants respectfully submit that this application claims priority back to provisional application Serial No. 60/247,088 filed November 10, 2000. Upon review of Moore et al., the provisional and the above-identified application disclosure, it will be apparent that the above-identified application predates Moore et al. Applicants respectfully request this rejection be withdrawn.

Claims 1-15 were rejected under 35 U.S.C. § 102(b) as being anticipated by Ostermeier et al.

Applicants traverse this rejection. Applicants respectfully submit that Ostermeier does not anticipate. A prior art publication for the same invention anticipates if the prior art publication discloses each and every limitation found in the claims either expressly or inherently.

*Rockwell Intern. Corp. v. U.S.*, 147 F.3d 1358, 1363 (Fed. Cir. 1998). Each claim limitation must be found in a single prior art references. Ostermeier fails to disclose the limitation of applying thermodynamics to a plurality of sequences to determine statistics of hybridization as disclosed and claimed in independent claims 1, 11 and 15. Ostermeier merely discloses using ITCHY and DNA shuffling to create the fusion libraries and sequencing positive clones from library and identifying "active" fusion points between the sequences and using kinetic characterization to look at the active hybrids. Conversely, Applicants disclose and claim a method wherein equilibrium thermodynamics is used to quantify conversions and selectivities that take place between the reassembled sequences (See claims 1, 11, and 15). As disclosed in the specification, the thermodynamics of duplex formation is analyzed by using nearest-neighbor parameters that describe the enthalpic and entropic contributions of specific nucleotide pairs in the overlapping region (see specification para. bridging pages 3 and 4; page 6, starting at 2<sup>nd</sup> para.). Such is not taught or disclosed by Ostermeier, therefore, Ostermeier fails to anticipate claims 1-15.

#### OBJECTION TO CLAIM

Claim 14 was objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Although not acceding to the Examiner's objections, Applicants have cancelled claim 14, thus making this objection moot.

## OBJECTION TO DISCLOSURE

The Examiner states that the disclosure is objected to because of the following informality:

The disclosure on page 17, line 6 contains a typographical/grammatical error:

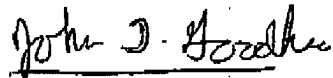
"...invention. only after...", wherein the word "only" requires capitalization.

Applicants have corrected the typographical/grammatical error on page 17, line 6 in the "Amendment to the Specification" section of this amendment.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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